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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,897	PELED ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *,9-14, 34-39 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,15-33 and 40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment, filed 4/11/03 (Paper No. 12), is acknowledged.

Claims 1-50 are pending.

Applicant's election of Group III, Claims 1-6, 8, 15-31, 33 and 40-49 and of neonatal umbilical cord blood as species of specific hematopoietic cells , tetraethylenepentamine (TEPA) as specific transition metal chelator, FLT3 ligand and G-CSF as specific early and late acting cytokine in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, the prior art search has been extended to include claims 7 and 32 since they both read on the elected cell population of hematopoietic or progenitor cell.

Claims 9-14, 34-39 and 50 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1- 8, 15- 33 and 40-49, as they all read on the elected species wherein neonatal umbilical cord blood is species of specific hematopoietic cells , tetraethylenepentamine (TEPA) is specific transition metal chelator, FLT3 and G-CSF is specific early and late acting cytokine are under consideration in the instant application.

2. The specification on page 1, line 15 should be amended to reflect the status of the parent applications 09/463,320 and 09/161,695. It is also noted that parent application 09/463,320 is a 371 not a continuation of PCT /IL99/00444.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1- 8, 15-33 and 40-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a CD4+ cell population cultured *ex-vivo* in a culture medium under conditions permitting said cell to proliferate and at the same time to reduce a capacity of said cells in utilizing copper, thereby expanding a population of said cells, while at the same time inhibiting differentiation of said cells does not reasonably provide **enablement** for *any* cell population cultured *ex-vivo* in a culture medium under conditions permitting said cell to proliferate and at the same time to reduce a capacity of said cells in utilizing copper, thereby expanding a population of said cells, while at the same time inhibiting differentiation of said cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses that providing $CD4^+$ cells *ex-vivo* with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper, only $CD4^+$ cells expanding and at the same time inhibiting differentiation (see examples 1 and 2 in particular).

The specification does not adequately teach how to effectively expand and at the same time inhibit differentiation of *any* cells by providing said cells ex-vivo with conditions for cell proliferation and at the same time for reducing a capacity of said cells in utilizing copper.

The specification does not teach how to extrapolate data obtained from $CD4^+$ cells *ex-vivo* assay studies to the development of effective protocols for imposing proliferation and at the same time restricting differentiation of *any* stem or progenitor cells by culturing said cells under conditions that reduces the capacity of said cells in utilizing copper. Moreover, Applicant himself acknowledge that the mechanism of the effects of cupper is unknown (see page 3, line 35-37 in particular). As such, the invention must be considered unpredictable. In addition, Percival (Am .J. Clin. Nutr. 1998, Vol.67 p.1064-1068) teaches that the role of copper in

effecting cellular function is contradictory and that more studies have to be done to understand the mechanisms by which copper effect the process of differentiation in various types of cells (see entire document, pages 1064 and 1066 in particular).

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed *any* cell population cultured *ex-vivo* in a culture medium under conditions permitting said cell to proliferate and at the same time to reduce a capacity of said cells in utilizing copper, thereby expanding a population of said cells, while at the same time inhibiting differentiation of said cells. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 1-8, 15-33 and 40-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : CD4+ cell population cultured *ex-vivo* in a culture medium under conditions permitting said cell to proliferate and at the same time to reduce a capacity of said cells in utilizing copper, thereby expanding a population of said cells.

Applicant is not in possession of : *any* cell population cultured *ex-vivo* in a culture medium under conditions permitting said cell to proliferate and at the same time to reduce a capacity of said cells in utilizing copper, thereby expanding a population of said cells, while at the same time inhibiting differentiation of said cells.

Applicant has disclosed a limited number of species of cell types; therefore, the skilled artisan cannot envision all the contemplated cell types recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of cell types may be achieved by means of a recitation of a representative number of cell types falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. The instant claims 6, 8, 18, 33 and 43 may not have the benefit under 35 U.S.C. § 120 of all of the parent filing dates. The subject matter claimed in Claims 6, 8 , 18, 33 and 43 that is a hematopoietic cells , wherein hematopoietic cells are obtained from neonatal umbilical cord blood and wherein transition metal chelator is tetraethylenepentamine dose not have a support in the parent applications Serial Numbers: 09/161/695, 09/130,367 and 09/024195.

If applicants disagree, applicants should present a detailed analysis as to why the claimed subject matter has clear support in the parent applications.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5, 17- 18, 24, 25-30, 42-43 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Percival et al. (J Nutrition, 1992, v122 pages 2424-2429)

Percival et al. teach culturing HL-60 cells in define growth medium condition that will stimulate growth while inhibit differentiation. (see entire document, Abstract in particular). Percival et al. teach that cells can be made copper deficient by incubating them in the media containing tetraethylenepentamine (TEPA), TEPA and zinc or TEPA and copper (see Abstact and Material and Methods in particular) . Percival et al. teach that copper is essential for the process of differentiation and chelating copper with tetraethylenepentamine will inhibit differentiation (see page 2428 in particular). Percival et al. teach that growth rate of HL-60

was not affected by TEPA , while TEPA did not allow differentiation. (see abstract in particular comprising HL- 60 cells.

Claims 4 and 5 and 28-29 are included because Percival et al. teach a cell population isolated from the growth medium and resuspended in PBS that is considered to be a pharmaceutical composition comprising the cells. (see Materials and Methods, page 2425 in particular).

Claims 25-27, 30 and 42-43 are included because the claimed functional limitation would be inherent properties of the referenced cell population because a cell population cultured ex-vivo in a culture medium under condition reducing a capacity of said cells in utilizing copper, will inherently result in a cell population having reduced intracellular copper content.

The reference teaching anticipates the claimed invention.

9. Claims 1- 8, 15- 17, 19-24 25- 33, 40-42 and 44-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Cicuttini et al. (Blood, 1992, Vol. 80 , pages 102-112)

Cicuttine et al. teach culturing hematopietic stem or progenitor cells using define growth condition that will stimulate growth while inhibit differentiation (see entire document, page 104, column 2 in particular). Cicuttine et al. teach isolating bone marrow cells from adults using methods known in the art (see page 103 in particular). The growth media containing nutrients, early and late acting cytokines (including G-CSF) and zinc, a transition metal chelator having an affinity for copper. Cicuttine et al. teach that zinc has an affinity to copper and would reduce copper utilization of culturing hematopoietic cells (see Discussion in particular). Therefore cells culturing the in the medium containing zinc would inherently reduces a capacity in utilizing cooper.

Cicuttine et al. teach isolating cell from cord blood which is considered equivalent to the neonatal umbilical cord blood in claims 8 and 33.

Claims 4 , 5 and 28-29 are included because Cicuttini et al.. teach a cell population isolated from the growth medium and resuspended in PBS that is considered to be a pharmaceutical composition comprising the cells. (see Materials and Methods, page 103 in particular).

Claims 25-27, 30 and 42-43 are included because the claimed functional limitation would be inherent properties of the referenced cell population because a cell population cultured ex-vivo in a culture medium under condition reducing a capacity of said cells in utilizing copper, will inherently result in a cell population having reduced intracellular copper content.

The reference teaching anticipates the claimed invention.

10. No claim is allowed.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 2, 2003.

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